UNITED STATES DISTRICT COURT

for the

District of New Jersey

IN RE: JOHNSON & JOHNSON TALCUM POWDER

Plaintiff

v.

PRODUCTS MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION

Defendant

Civil Action No. 3:16-md-2738-MAS-RLS

SUBPOENA TO PRODUCE DOCUMENTS, INFORMATION, OR OBJECTS OR TO PERMIT INSPECTION OF PREMISES IN A CIVIL ACTION

To: Northwell Health, Inc. (attn: Custodian of Records)
2000 Marcus Ave., New Hyde Park, NY 11042-1069

(Name of person to whom this subpoena is directed)

☑ *Production:* **YOU ARE COMMANDED** to produce at the time, date, and place set forth below the following documents, electronically stored information, or objects, and to permit inspection, copying, testing, or sampling of the material:

All documents set forth on Schedule A.

Place:	Date and Time:
Faegre Drinker Biddle & Reath LLP 600 Campus Drive, Florham Park, New Jersey 07932	01/02/2024 10:00 am

☐ *Inspection of Premises:* **YOU ARE COMMANDED** to permit entry onto the designated premises, land, or other property possessed or controlled by you at the time, date, and location set forth below, so that the requesting party may inspect, measure, survey, photograph, test, or sample the property or any designated object or operation on it.

Place:	Date and Time:

The following provisions of Fed. R. Civ. P. 45 are attached – Rule 45(c), relating to the place of compliance; Rule 45(d), relating to your protection as a person subject to a subpoena; and Rule 45(e) and (g), relating to your duty to respond to this subpoena and the potential consequences of not doing so.

Date: 12/13/2024

CLERK OF COURT

OR

Susan Sharko

Signature of Clerk or Deputy Clerk *Attorney's signature*

The name, address, e-mail address, and telephone number of the attorney representing *(name of party)* Defendant Johnson & Johnson, who issues or requests this subpoena, are:
Susan M. Sharko, Esq., 600 Campus Drive, Florham Park, New Jersey 07932, susan.sharko@faegredrinker.com, (973) 549-7350

Notice to the person who issues or requests this subpoena

If this subpoena commands the production of documents, electronically stored information, or tangible things or the inspection of premises before trial, a notice and a copy of the subpoena must be served on each party in this case before it is served on the person to whom it is directed. Fed. R. Civ. P. 45(a)(4).

Federal Rule of Civil Procedure 45 (c), (d), (e), and (g) (Effective 12/1/13)

(c) Place of Compliance.

(1) ***For a Trial, Hearing, or Deposition.*** A subpoena may command a person to attend a trial, hearing, or deposition only as follows:

(A) within 100 miles of where the person resides, is employed, or regularly transacts business in person; or

(B) within the state where the person resides, is employed, or regularly transacts business in person, if the person

(i) is a party or a party's officer; or

(ii) is commanded to attend a trial and would not incur substantial expense.

(2) ***For Other Discovery.*** A subpoena may command:

(A) production of documents, electronically stored information, or tangible things at a place within 100 miles of where the person resides, is employed, or regularly transacts business in person; and

(B) inspection of premises at the premises to be inspected.

(d) Protecting a Person Subject to a Subpoena; Enforcement.

(1) ***Avoiding Undue Burden or Expense; Sanctions.*** A party or attorney responsible for issuing and serving a subpoena must take reasonable steps to avoid imposing undue burden or expense on a person subject to the subpoena. The court for the district where compliance is required must enforce this duty and impose an appropriate sanction—which may include lost earnings and reasonable attorney's fees—on a party or attorney who fails to comply.

(2) ***Command to Produce Materials or Permit Inspection.***

(A) *Appearance Not Required.* A person commanded to produce documents, electronically stored information, or tangible things, or to permit the inspection of premises, need not appear in person at the place of production or inspection unless also commanded to appear for a deposition, hearing, or trial.

(B) *Objections.* A person commanded to produce documents or tangible things or to permit inspection may serve on the party or attorney designated in the subpoena a written objection to inspecting, copying, testing, or sampling any or all of the materials or to inspecting the premises—or to producing electronically stored information in the form or forms requested. The objection must be served before the earlier of the time specified for compliance or 14 days after the subpoena is served. If an objection is made, the following rules apply:

(i) At any time, on notice to the commanded person, the serving party may move the court for the district where compliance is required for an order compelling production or inspection.

(ii) These acts may be required only as directed in the order, and the order must protect a person who is neither a party nor a party's officer from significant expense resulting from compliance.

(3) ***Quashing or Modifying a Subpoena.***

(A) *When Required.* On timely motion, the court for the district where compliance is required must quash or modify a subpoena that:

(i) fails to allow a reasonable time to comply;

(ii) requires a person to comply beyond the geographical limits specified in Rule 45(c);

(iii) requires disclosure of privileged or other protected matter, if no exception or waiver applies; or

(iv) subjects a person to undue burden.

(B) *When Permitted.* To protect a person subject to or affected by a subpoena, the court for the district where compliance is required may, on motion, quash or modify the subpoena if it requires:

(i) disclosing a trade secret or other confidential research, development, or commercial information; or

(ii) disclosing an unretained expert's opinion or information that does not describe specific occurrences in dispute and results from the expert's study that was not requested by a party.

(C) *Specifying Conditions as an Alternative.* In the circumstances described in Rule 45(d)(3)(B), the court may, instead of quashing or modifying a subpoena, order appearance or production under specified conditions if the serving party:

(i) shows a substantial need for the testimony or material that cannot be otherwise met without undue hardship; and

(ii) ensures that the subpoenaed person will be reasonably compensated.

(e) Duties in Responding to a Subpoena.

(1) ***Producing Documents or Electronically Stored Information.*** These procedures apply to producing documents or electronically stored information:

(A) *Documents.* A person responding to a subpoena to produce documents must produce them as they are kept in the ordinary course of business or must organize and label them to correspond to the categories in the demand.

(B) *Form for Producing Electronically Stored Information Not Specified.* If a subpoena does not specify a form for producing electronically stored information, the person responding must produce it in a form or forms in which it is ordinarily maintained or in a reasonably usable form or forms.

(C) *Electronically Stored Information Produced in Only One Form.* The person responding need not produce the same electronically stored information in more than one form.

(D) *Inaccessible Electronically Stored Information.* The person responding need not provide discovery of electronically stored information from sources that the person identifies as not reasonably accessible because of undue burden or cost. On motion to compel discovery or for a protective order, the person responding must show that the information is not reasonably accessible because of undue burden or cost. If that showing is made, the court may nonetheless order discovery from such sources if the requesting party shows good cause, considering the limitations of Rule 26(b)(2)(C). The court may specify conditions for the discovery.

(2) ***Claiming Privilege or Protection.***

(A) *Information Withheld.* A person withholding subpoenaed information under a claim that it is privileged or subject to protection as trial-preparation material must:

(i) expressly make the claim; and

(ii) describe the nature of the withheld documents, communications, or tangible things in a manner that, without revealing information itself privileged or protected, will enable the parties to assess the claim.

(B) *Information Produced.* If information produced in response to a subpoena is subject to a claim of privilege or of protection as trial-preparation material, the person making the claim may notify any party that received the information of the claim and the basis for it. After being notified, a party must promptly return, sequester, or destroy the specified information and any copies it has; must not use or disclose the information until the claim is resolved; must take reasonable steps to retrieve the information if the party disclosed it before being notified; and may promptly present the information under seal to the court for the district where compliance is required for a determination of the claim. The person who produced the information must preserve the information until the claim is resolved.

(g) Contempt.

The court for the district where compliance is required—and also, after a motion is transferred, the issuing court—may hold in contempt a person who, having been served, fails without adequate excuse to obey the subpoena or an order related to it.

For access to subpoena materials, see Fed. R. Civ. P. 45(a) Committee Note (2013).

SCHEDULE A

A. The terms "you," and/or "your" shall mean Northwell Health, Inc. ("Northwell") including without limitation any agents, representatives, attorneys, investigators, insurers, employees, brokers, independent contractors, subcontractors, and/or any person, persons, entity or entities or persons acting on the behalf of the aforesaid.

B. The terms "and" and "or" shall be construed either conjunctively or disjunctively as necessary to bring within the scope of these requests any relevant information that might otherwise be construed to be outside the scope of requests.

DOCUMENTS REQUESTED

1. An unredacted copy of the five-page key identifying the plaintiffs that Dr. Moline chose to include in her article Moline J, Bevilacqua K, Alexandri M, Gordon RE. Mesothelioma Associated With the Use of Cosmetic Talc. J OCCUP ENVIRON MED. 2020 Jan;62(1): 11-17. Doi: 10.1097/JOM.0000000000001723, including Erratum in: J OCCUP ENVIRON MED. 2023 May 1;65(5):e362. PMID: 31609780.

    a. Attached hereto as **Exhibit A** is a copy of Moline J, Bevilacqua K, Alexandri M, Gordon RE. Mesothelioma Associated With the Use of Cosmetic Talc. J OCCUP ENVIRON MED. 2020 Jan;62(1): 11-17. Doi: 10.1097/JOM.0000000000001723, including Erratum in: J OCCUP ENVIRON MED. 2023 May 1;65(5):e362. PMID: 31609780.
    b. Attached hereto as **Exhibit B** is a redacted copy of the five-page key identifying the plaintiffs that Dr. Moline chose to include in her article

2. An unredacted copy of the key identifying the plaintiffs that Dr. Moline chose to include in her article Moline J, Patel K, Frank AL. Exposure to cosmetic talc and mesothelioma. J OCCUP MED TOXICOL. 2023 Jan 18; 18(1):1. Doi: 10.1186/s12995-023-00367-5. PMID: 36653798; PMCID: PMC9847157.

    a. Attached hereto as **Exhibit C** is a copy of Moline J, Patel K, Frank AL. Exposure to cosmetic talc and mesothelioma. J OCCUP MED TOXICOL. 2023 Jan 18; 18(1):1. Doi: 10.1186/s12995-023-00367-5. PMID: 36653798; PMCID: PMC9847157.

EXHIBIT A

Mesothelioma Associated With the Use of Cosmetic Talc

Jacqueline Moline, MD, MSc, Kristin Bevilacqua, MPH, Maya Alexandri, JD, and Ronald E. Gordon, PhD

Objective: To describe 33 cases of malignant mesothelioma among individuals with no known asbestos exposure other than cosmetic talcum powder. **Methods:** Cases were referred for medico-legal evaluation, and tissue digestions were performed in some cases. Tissue digestion for the six cases described was done according to standard methodology. **Results:** Asbestos of the type found in talcum powder was found in all six cases evaluated. Talcum powder usage was the only source of asbestos for all 33 cases. **Conclusions:** Exposure to asbestos-contaminated talcum powders can cause mesothelioma. Clinicians should elicit a history of talcum powder usage in all patients presenting with mesothelioma.

BACKGROUND

Asbestos in all forms is recognized by the International Agency for Research on Cancer (IARC) as a human carcinogen and all forms of asbestos are recognized as the primary risk factor for malignant mesothelioma.[1–9] By the mid-1950s, over 60 cases of asbestos-related lung cancer had been published in the literature. In 1955, Doll[10] published a seminal paper describing the increased risk of lung cancer among asbestos-exposed workers. In 1960, Wagner et al[2] published a study of 33 cases of malignant mesothelioma among individuals who were exposed to asbestos in and around the crocidolite mines in South Africa. By the mid-20th century, as asbestos use rose in the industrialized world, diseases associated with its use also began their upward curve.[3,8,11,12] On average between 2003 and 2008 1.05 cases per 100,000 of malignant mesothelioma (MM) were diagnosed in the United States and in 2015, 2597 deaths resulted from the disease.[13,14]

The presence of asbestos in talc and talcum powder consumer products including body powder, baby powder, facial cosmetics, and pharmaceutical talc was first discussed in the medical and scientific literature beginning in the 1940s.[15–17] Asbestos contamination of talc products is understood to occur during the mining process, in which talc deposits overlap or lie in close proximity to naturally occurring asbestos deposits.[18–22] The natural presence of asbestos within talc deposits makes selective mining or the extrication of asbestos from mined talc nearly impossible.[19] During application in its commercial talcum powder form, asbestos fibers become airborne and can be inhaled.[23,24] In 1968, Cralley et al[25] found the presence of three different types of asbestos fibers in 22 of 22 talcum products tested (tremolite, anthophyllite, and chysotile). However, talcum powder is still widely produced and consumed with a reported 58.3 million adults using body and baby powder in the United States in 2017.[26]

While the relationship between occupational exposure to asbestos and mesothelioma is well established, multiple studies have shown that not all individuals who develop mesothelioma can pinpoint exposures to asbestos.[8,11] Among women, occupational exposure explains less than half of malignant mesothelioma cases.[27,28] Some studies have focused on conventional exposure categories that for women only reflect take home exposures from (male) family members who worked in one of the selected occupations. In one such study, data on home or personal use exposures were not collected, yet increased amounts of tremolite asbestos fibers noted in the lungs of women with MM with no identified source of asbestos contact led study authors to hypothesize that the tremolite could be related to talcum powder use.[28] The high prevalence of unexplained or, ''idiopathic mesothelioma'' among women necessitates further inquiry into potential non-occupational exposures, such as exposure to asbestos-contaminated talcum powder.

In light of these gaps in the existing literature, we present 33 cases of individuals with malignant mesothelioma who were exposed to commercial talcum powder products. Of those cases, we present six in detail, where the individuals had no other known exposure to asbestos and for whom tissue studies show the presence of asbestos commonly found in talcum powder (such as tremolite, and/or anthophyllite). For all 33 cases, other potential exposures to asbestos were considered, with no identified source apart from the talcum powder. The cases were referred to author J.M. for medico-legal evaluation as part of tort litigation, and tissue digestions were performed by author R.G. as part of this litigation. In every case, a pathology report confirmed the diagnosis of malignant mesothelioma. This study was conducted with approval from the Northwell Health Feinstein Institute for Medical Research (#18-0225 FIMR).

MATERIALS AND METHODS

Case Histories

Data gathered for all 33 patients were gathered from each individual's medical records and sworn testimony (deposition transcripts) of individuals. All cases were reviewed by an occupational physician with experience evaluating asbestos exposure in thousands of patients. Data abstracted included medical diagnosis, review of pathology reports confirming the diagnosis of malignant mesothelioma, and clinical course. Exposure data was obtained from sworn testimony by the cases, which included extensive questioning regarding all sources of asbestos exposure. This included family occupational histories (parents and anyone cohabitating with the patient) for all cases to assess potential asbestos exposure, hobbies that included use of products that might contain asbestos (such as ceramics), residence in an area that might have had asbestos industry leading to possible environmental exposures, known abatement of asbestos while the patient was in school, home renovations that might have used asbestos containing materials, and any other potential sources of asbestos exposure. Additional data related to family history of cancers was obtained from the sworn testimony. Any data related to potential genetic mutations such as BRCA1 associated protein-1 was collected, if present.

From the Northwell Health Department of Occupational Medicine Epidemiology and Prevention (Dr Moline, Ms Bevilacqua); Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead (Ms Alexandri); Department of Pathology, The Icahn School of Medicine at Mount Sinai (Dr Gordon), New York, New York.

Funding: No funds or external assistance were obtained by any outside source in the development, writing, analysis, or conclusions of this manuscript.

Conflicts of Interest: Authors J.M. and R.G. have served as expert witnesses in asbestos litigation, including talc litigation for plaintiffs.

Supplemental digital contents are available for this article. Direct URL citation appears in the printed text and is provided in the HTML and PDF versions of this article on the journal's Web site (www.joem.org).

Clinical Significance: This manuscript is the first to describe mesothelioma among talcum powder consumers. Our case study suggest that cosmetic talcum powder use may help explain the high prevalence of idiopathic mesothelioma cases, particularly among women, and stresses the need for improved exposure history elicitation among physicians.

Address correspondence to: Jacqueline Moline, MD, Northwell Health, Great Neck, NY (jmoline@northwell.edu).

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Talcum powder exposure histories were reviewed based on sworn testimony by patients and in some cases, family members with first-hand knowledge of the use of talcum powder, such as parents who recalled using talcum powder while diapering the patient. Data including type of talcum powder used (Appendix 3, http://links.lww.com/JOM/A651), age at first use of talcum powder, and duration of use was obtained to ensure adequate latency from first exposure was present.[29] In some cases, individuals were also interviewed in person, and these data were merged with the data obtained in medical records and deposition transcripts.

The six cases described below also had tissue digestions performed by author R.G. These case reports are presented in greater detail; their clinical course was similar to all 33 cases evaluated, and the same rigor with respect to obtaining information related to any asbestos exposure was applied to all 33 cases.

Case 1

Case 1 is a 70-year-old woman who presented to a physician with shortness of breath and chest pain in January 2015. A chest x-ray revealed a small pleural effusion with left basilar atelectasis. In August 2015, a CT angiogram showed development of two subpleural nodules anterior to the lingula and a pleural based mass; a pleural effusion was still present. A thoracentesis was done and the cytology showed large clusters of cells suspicious for mesothelioma. A positron emission tomography (PET) scan showed pleural thickening and focal intense uptake inferiorly and posteriorly on the left side of her chest. In September 2015, she underwent thoracoscopic surgery. The pathology showed epithelial malignant mesothelioma with invasion of the visceral pleura and pulmonary parenchyma with tumor present at the stapled margin.

Case 1 applied loose face powder on a daily basis from the 1940s to the 1970s. Her mother also used the same loose face powder and Case 1 cleaned residual powder from her mother's dresser and clothing every other week from 1994 to 2012.

Electron microscopic analysis (EMA) of the lung tissue revealed anthophyllite fibers in a calculated concentrations of 3286 fibers per gram weight. There was also significant amount of fibrous and platy talc and aluminum silicates.

Case 1 was treated with four cycles of combination chemotherapy with cisplatin and pemetrexed for four cycles.

Case 2

In August 2015, Case 2, a 65-year-old woman presented with exertional dyspnea and dry cough. A chest x-ray showed a large left pleural effusion. A chest CT scan in September 2015 showed a freely-movable, large-volume, left pleural effusion, nodularity/lobulation of the left pleura, left lower lobe atelectasis, three nodules in the left upper lobe, and no hilar or mediastinal lymphadenopathy. A thoracentesis showed carcinoma cells. A PET-CT scan on September 22, 2016 reported showed abnormal deposits of tumor in the left pleura. There was no reported disease outside the chest.

Case 2 underwent a bronchoscopy in October, 2015. Pathology showed malignant mesothelioma, biphasic mixed type (50% sarcomatoid, 50% epithelioid). A second opinion confirmed the diagnosis. She underwent two cycles of chemotherapy with doxorubricin, ifosfide, and mensa and completed treatment in November. A PET scan showed no response to the chemotherapy. In December, Case 2 underwent left radical pleurectomy/decortication, resection of left hemidiaphragm, and one lymph node dissection. Surgical pathology showed residual biphasic malignant mesothelioma with negative nodes and negative margins. In January 2016, radiation oncology recommended adjuvant radiation therapy to the left chest, which she received in February and March of 2016. As of April 2016, Case 2 had no evidence of disease recurrence.

Case 2 reported starting to use talc around age eight or nine and would apply powder after her daily shower or bath. She would also use talcum powder when visiting her grandmother because she enjoyed the scent and would apply the powder before going on a date. She continued to use powder after getting married and used baby powder with all three of her children. In the early 2000s she began to regularly apply a fragrance and its matching talcum powder in the morning and at night, describing it as her signature scent. She also sprinkled the powder in her lingerie drawer and traveled with the powder which she would rub on her suitcases and other surfaces.

EMA of the lung tissue revealed anthophyllite fibers in a calculated concentration of 8625 fibers per gram wet weight with a limit of detection of 2875 fibers per gram wet weight. A significant amount of fibrous and platy talc was seen. EMA of the lymph node tissue revealed anthophyllite and tremolite fibers in a calculated concentrations of 34,500 fibers per gram wet weight with a limit of detection of 11,500 fibers per gram wet weight. They were seen in a ratio of 2:1 anthophyllite:tremolite/actinolite. All fibers counted were 5 μm or greater in length with aspect ratios greater than 8. There was also some amount of fibrous and platy talc noted in the lymph node tissue.

Case 3

In September 2014, Case 3, an 84-year-old woman, developed shortness of breath, a cough, and chest tightness. A chest x-ray in November 2014 showed a large left pleural effusion. A CT angiogram showed a large left pleural effusion with compressive atelectasis of the left middle and lower lobes and ground glass opacities in the left upper lobe and right lung. A thoracentesis showed carcinoma cells. Case 3 underwent a video thoracoscopy with pleural biopsy and evacuation of a pleural effusion. Pathology revealed a malignant epithelial neoplasm consistent with malignant epithelial mesothelioma. Case 3 then underwent a left pleurectomy and decortication in June 2015. The mesothelioma had spread to the lymph nodes and chest wall, and the pathology now showed malignant biphasic mesothelioma. Case 3 entered hospice care in September 2015 and died in late October 2015.

Case 3 worked as an elementary school teacher with no known occupational exposure to asbestos. Case 3 used talcum powder ''before [she] was 12 and 13 years old,'' applying it under her arms and in her shoes daily. She shook the powder out of the can and applied it onto her body. She noted that her mother also used talcum body powder, and they shared a small bathroom. She used talcum powder beginning in the 1940s and continuing for decades, until her preferred brand was no longer available for purchase.

EMA of the lung tissue did not reveal any asbestos fibers above the limit of detection of 6900. However, there were a number of very small chrysotile asbestos fibers. Analysis of the lymph node tissue revealed tremolite asbestos fibers in calculated concentrations of 9409 fibers per gram wet weight with a limit of detection of 9409. All fibers counted were 5 μm or greater in length with aspect ratios greater than 20. There was also a significant amount of aluminum silicates, silica particles, and both fibrous and platy talc. Light microscopic analysis revealed a calculated concentration of 409 asbestos bodies per gram wet weight of lymph node tissue by phase contrast light microscopy.

Case 4

In August 2014, Case 4, a 66-year-old woman, developed abdominal pain and had a CT scan of the abdomen and pelvis that showed omental caking, ascites, a fluid pocket in the right lower quadrant, and enlarged diaphragmatic lymph nodes. She underwent a paracentesis and an omental biopsy in August 2014. The cytology revealed atypical mesothelial cells. She then underwent a laparotomy, appendectomy, omentectomy, and left salpingo-oophorectomy. The pathology showed malignant epithelioid mesothelioma. In September 2014, a PET/CT showed increased uptake in the abdomen consistent with malignant ascites, omental metastatic disease, and cardiophrenic

nodules. A thoracoscopy showed tumor covering the right hemidiaphragm. She was treated with multiple rounds of chemotherapy with cisplatin and pemetrexed and therapeutic paracenteses due to persistent ascites. Her tumor progressed, and she died in February 2016. She was 68 years old.

Case 4 grew up in a home where her mother used talcum powder "for as long as [she could] remember." She recalled personally using talcum powder starting around the age of 9 or 10, applying the powder to her armpits, groin, and around her body, using a powder puff. She applied talcum powder to her body for approximately 40 years. Case 4 had additional exposure to talcum powder in the 1960s while working as a licensed cosmetologist, applying talcum powder on clients' necks after a haircut. She shook the talcum powder onto the client's neck, and would wipe off the excess with a brush or blow dryer. She also used talcum powder inside the gloves that she donned prior to applying hair color.

EMA of the peritoneal tissue revealed chrysotile type asbestos fibers in a calculated concentration of 920 fibers per gram wet weight with a limit of detection of 920 fibers per gram wet weight. Fibrous and platy talc was also observed. Also seen were non-asbestiform tremolite and silica crystals.

Case 5

Case 5 was a 76-year-old woman who developed chest pain and fatigue in September 2015 and was diagnosed with viral pericarditis. A CT scan in October 2015 showed mild pericardial thickening and mild perihepatic ascites. She was treated with steroids for viral pericarditis. In late fall 2015, Case 5 developed decreased appetite, weight loss, tenderness around the umbilicus, and abdominal pain. In December 2015 she had an abdominal ultrasound that showed a mild to moderate amount of ascites. An abdominal CT scan showed slightly bilateral pleural thickening with minimal linear atelectatic change. There was copious perihepatic ascites extending to the right and left paracolic gutter and deep pelvis, nodularity at the paracolic gutter, and a right sided deep pelvic mass. A paracentesis was done and showed atypical epithelioid cells and tissue fragments with an inflammatory background. A laparoscopy showed peritoneal carcinomatosis with a diffuse miliary excrescence, a moderate sized pelvic mass and ascites. In January 2016 she underwent an exploratory laparotomy and resection of the omentum, spleen, resection of abdominal tumor, and resection of the abdominal wall tumor. The pathology showed malignant mesothelioma involving the omentum, spleen, colon, and mesentery, as well as the fibroadipose tissue of the peritoneum. Malignant mesothelioma also involved the parietal peritoneum as well as the appendix, with fibrous obliteration of the appendiceal lumen. Case 5 died in October 2017.

Case 5 had daily personal use of talcum body powder from the 1950s to the mid-1970s. She would pour the powder onto her hands and pat it under her arms, in her genital area, between her toes, and on her legs. When she was menstruating she would apply talcum powder on her feminine napkins and her underwear. She also applied talcum powder to her shoes. Case 5's husband also used talcum powder. Both Case 5 and her husband applied the powder in the bathroom. She shook the bathroom floor mat and cleaned up residual powder from the bathroom sink.

EMA of the omental tissue did not reveal any asbestos fibers above the limit of detection of detection of 651 fibers per gram wet weight. EMA of the lymph node tissue revealed chrysotile and anthophyllite asbestos fibers in a calculated concentrations of 20,700 fibers per gram wet weight with a limit of detection of 10,350 fibers per gram wet weight. All fibers counted were 5 μm or greater in length with aspect ratios greater than 20. There was also a significant amount of fibrous and platy talc as well as fibrous and platy aluminum silicates.

Case 6

Case 6 is a 44-year-old man who developed chest pain after playing hockey in 2012 and was evaluated in the Emergency Department. A CT scan that showed no pulmonary abnormalities. Case 6 continued to have chest pain over the next 4 years and underwent multiple cardiac evaluations. A CT scan in February 2016 showed increased pleural thickening or non-calcified pleural plaque along the right major fissure and anterior right hemithorax along the right upper lobe. A PET/CT scan in March 2016 showed unilateral hypermetabolic pleural fissural and non-fissural soft tissue abnormalities suspicious for malignancies involving the pleura. There were non-specific tiny parenchymal lung nodules. Case 6 underwent a tissue biopsy in March 2016. The pathology showed malignant epithelioid mesothelioma with invasion to the skeletal muscle.

Case 6 underwent neo-adjuvant chemotherapy with pemetrexed, cisplatin, and bevacizumab in April 2016. In May 2016, Case 6 underwent a mediastinoscopy which showed metastatic spread to the level VII lymph node. Additional chemotherapy was administered, which was not well tolerated. In July 2016, a parietal pleurectomy was done along the fissure between the upper and lower lobe. There was spread to the site of previous inferior right chest tube site. Case 6 developed acute thrombus in the right upper extremity. In September 2016, a chest x-ray showed unchanged right pleural thickening versus a small right pleural effusion. Three additional cycles of chemotherapy were recommended. A PET/CT scan in November 2017 showed a persistent hypermetabolic focus in the right anterobasal pleura and a slight increase in a right pleural effusion.

Case 6 was exposed to talcum powder beginning when he was an infant. His mother applied it to him after his bath until he was able to apply it himself, starting around the age of six. Case 6 recalled using the powder in the bathroom and in his room, and that there would be powder on his floor. He applied the talcum powder directly to his torso, groin, legs, and back, often twice a day after showering. He played hockey as a youth and used powder in his hockey gear before donning the equipment. He recalled getting mouthfuls of powder during the application. He often applied talcum powder once or twice a day after showering. He had no occupational exposure to asbestos.

EMA of the lymph node tissue revealed anthophyllite and tremolite asbestos fibers in a calculated concentrations of 17,250 fibers per gram wet weight with a limit of detection of 3450 fibers per gram wet weight. They were seen in a ratio of 2:3 anthophyllite:tremolite. All fibers counted were 5 μm or greater in length with aspect ratios greater than 14.7 or greater. There was also some amount of fibrous and platy talc along with platy aluminum silicates and magnesium aluminum silicates.

Tissue Sample Analysis

Tissue samples from six patients were analyzed: (a) lung and lymph node tissue from four of the patients diagnosed with pleural mesothelioma; and (b) lung and lymph node from two of the patients diagnosed with peritoneal mesothelioma. The tissue samples had been preserved in paraffin blocks or as formalin fixed tissues.

Tissue Digestion Protocols

Paraffin Blocks

The tissue was extracted from paraffin blocks was done according to the methodology described in Heller et al[30] and Wu et al.[31] The tissues were cut from the paraffin blocks and deparaffinized by melting and xylene treatment. They were brought to water, blotted and weighted. The tissues were digested with KOH and the inorganic pellet cleaned with distilled water by multiple centrifugation steps on an asbestos locator grid coated with formvar. In

addition, 250 μL samples were prepared using a cytocentrifuge onto a standard glass slide to identify ferruginous bodies and longer fibers by phase contrast microscopy.

Formalin Fixed Tissue

This protocol is similar to above without the deparaffinizing step as described in [23,39]. Controls for both the paraffin and formalin fixed tissues included looking at the paraffin, if from blocks, the formalin, if from fixed wet tissue, or any other materials used to process the tissue to view the remaining inorganic material on the grids.

Asbestos Fiber Counting

The grids were analyzed two ways: (a) transmission electron microscopy (TEM) using a standard fiber-counting protocol (23,40)[23,32] on 800 grid openings; and (b) phase contrast light microscopy on two cytocentrifuge preparations per tissue type in accordance with a standard asbestos body-counting protocol (23,40).[23,32] Asbestos fibers were evaluated to determine whether they met the definition of a fiber, which includes having at a 5:1 length:width ratio and parallel sides and at least 5 μm in length. The fibers were also analyzed by Energy Dispersive Spectroscopy (EDS) to determine the ratio of elements contained in the fibers and by Selected Area Electron Diffraction (SAED) to confirm the crystalline structure of the fiber to confirm that they were asbestos. To evaluate for potential contamination, control samples were prepared from the same distilled water used to wash the samples and the paraffin surrounding the tissue. Verification techniques of fiber counting were used for quality control and quality assurance. All fibers, regardless of size, were counted in 800 grid openings.

Calculating Asbestos Fiber Concentration

TEM and PCM

Asbestos fiber concentration in the samples examined with transmission electron microscopy was calculated (see Appendix 1, http://links.lww.com/JOM/A649). The 250 μL samples centrifuged onto standard microscope slides were examined using phase contrast light microscopy (Appendix 2, http://links.lww.com/JOM/A650). The asbestos fiber concentration in these samples was calculated (see Appendix 2, http://links.lww.com/JOM/A650).

Control Samples

Background control samples were obtained at autopsy or from surgical specimens from pulmonary or obstetrical and gynecologic pathologists. Samples included lung, thoracic, mesenteric and abdominal lymph nodes, abdominal tissue, ovaries, fallopian tubes, uteri and mesentery tissue. Exposure histories had been obtained by treating pulmonologists or surgeons from all individuals; all were screened for asbestos exposure from personal use, family exposure, and personal or family use of talcum powder. For those patients in whom there was any question of asbestos exposure from any source, the pathologists conferred with the treating clinician to ensure there was no known asbestos exposure. If there was potential asbestos exposure, the specimens were not included in the group. As a result, the background control specimens reflect only asbestos exposure from the overall community.

RESULTS

The data associated with the exposure history of all 33 patients is presented in Table 1. The table identifies talcum powder as the only asbestos exposure these patients have experienced. No individual identified any asbestos exposure apart from contaminated talcum powder from workplace or household exposures.

Table 2 provides the results of the fiber burden analyses for the six cases in which asbestos fibers were identified in the anatomic vicinity of the patients' mesotheliomas. Uniformly, the tissue fiber burdens reveal the presence of the following: talc, aluminum silicates, aluminum magnesium silicates, silica crystals, and asbestos fibers. The asbestos fibers are all anthophyllite, tremolite, and/or chrysotile. These three types are typical contaminants of talcum powders.[19] They have been identified as contaminants in talcum powders in repeated laboratory testing at numerous institutions.[33–37] The tissue fiber burdens contained no amosite or crocidolite, commercial amphibole asbestos fibers. Testing results of talcum powders have failed to show the presence of commercial amphiboles.

Table 3 presents the asbestos fiber burden results from background controls in tissues from autopsy and surgical population with no evidence of ovarian cancer or other malignancy, and with no known asbestos exposure. The lung and lymph nodes sampled showed only chrysotile and non-commercial amphibole asbestos in a small percentage of control samples—six of the 35 control samples, or 17%. All women with asbestos present were over 60 years of age. While asbestos is present at extremely low concentrations in the ambient air,[38] in the control samples presented in the study, there was no evidence of asbestos in women under the age of 60 years of age. Two fibers were seen in two specimens and one fiber was seen in four samples, all under 1 μm in size. The asbestos fiber burdens in the six talc exposed patients were all greater than the control population. No aluminum silicates, aluminum magnesium silicates, and silica crystals, all components of talcum powder identified in our patients, were not found in the control population that did not use talcum powder.

DISCUSSION

This paper provides the first large case series to identify cosmetic talcum powder contaminated with asbestos as the cause of malignant mesothelioma in cosmetic talc users. In 1960, Wagner presented 33 individuals exposed to crocidolite asbestos from occupational and environmental exposures, providing the first large case series of individuals diagnosed with mesothelioma with clearly identifiable exposure to asbestos.[2] Since then, the high prevalence of idiopathic mesothelioma cases suggested other possible exposures, including exposure to asbestos contaminated talc. Like Wagner, we present 33 cases, predominantly of women, who had no known exposure to asbestos other than prolonged use of talcum powder. This is consistent with the distribution of talcum powder usage in the United Sates, with greater numbers of women using powder than men.[26] Furthermore, the six case histories detailed years or decades of talcum powder use as well as tissue analysis that showed asbestos present in either tumor tissue or lymph nodes. In all six cases, asbestos fibers consistent with those identified as contaminants in repeated laboratory testing of talcum powder samples across several institutions were identified.[20,23,33,39] Notably, the fiber types found were consistent with the types of asbestos found in talc. Amosite and crocidolite, asbestos fibers that are encountered in cases of industrial and occupational exposure, not cosmetic talcum powder,[40] were not found in any of these cases.

This paper is also the first, to the authors' knowledge, to utilize background controls for which an extensive exposure history was elicited and for which no known asbestos exposure had occurred. Background controls are the best comparison when analyzing tissue of asbestos exposed individuals however, one of the biggest challenges is to choose a population of patients with no history of environmental or occupational exposure to asbestos apart from ambient air concentration of asbestos. Previous fiber burden studies of non-occupationally exposed individuals have compared the asbestos content in their tissue to workers in the same community where asbestos mines or asbestos containing factories were

TABLE 1. Description of 33 Mesothelioma Cases

Talcum Powder Exposure

Case	Sex	Year of Diagnosis	Age at Diagnosis	Mesothelioma Site	Histology	Talcum Powder Brand	Estimated Years of Use	Occupation (s)
1*	F	2015	70†	Pleural	Epithelial	A	30	Medical technician
2*	F	2015	65	Pleural	Biphasic	C, H, V	50	Homemaker
3*	F	2014	82†	Pleural	Biphasic	C	70	Teacher
4*	F	2014	66†	Peritoneal	Epithelial	B, C	30	Hairdresser
5*	F	2015	75†	Peritoneal	Epithelial	C	25	Teacher
6*	M	2016	43	Pleural	Epithelial	D	40	Finance
7	M	2016	65	Peritoneal	Epithelial	D	62	None provided
8	M	2016	76†	Pleural	Epithelial	U	38	Accountant
9	F	2016	66†	Pleural	Epithelial	C, E	35	Hair dresser
10	F	2015	80	Pleural	Epithelial	F	30	Administrative assistant
11	F	2018	73	Pleural	Epithelial	C, V	30	Flight attendant
12	F	2017	57	Peritoneal	Epithelial	A, D, G, H, I	40	Medical technologist
13	M	2016	56	Peritoneal	Biphasic	D, I, S	15	Maintenance worker
14	M	2017	56	Peritoneal	Epithelial	D	50	Molding press operator
15	F	2016	40	Peritoneal	Epithelial	D, J	12	Retail worker
16	F	2015	30	Pleural	Epithelial	D, K, L, M	19	Retail worker
17	F	2015	80†	Pleural	Epithelial	A, C, N	40	Office worker
18	F	2015	64	Pleural	Sarcomatoid	C	40	Real Estate agent
19	F	2009	62	Pleural	Epithelial	C	15	Teacher and fitness instructor
20	F	2016	69	Peritoneal	Epithelial	D, G	30	Hair dresser
21	F	2013	34†	Peritoneal	Epithelial	C	10	Teacher
22	F	2018	59	Pleural	Epithelial	C, D	42	School custodian
23	F	2016	27	Peritoneal	Epithelial	D, O	10	Not provided
24	F	2016	38	Peritoneal	Epithelial	D, I	18	Social services
25	F	2017	64	Pleural	Epithelial	D, G, J	27	Mathematician
26	F	2016	83	Pleural	Epithelial	C, D, I	60	Not provided
27	F	2017	41	Peritoneal	Epithelial	D	30	Computer programmer
28	F	2016	79	Peritoneal	Epithelial	A, C, T,	21	Not provided
29	M	2015	46	Pleural	Epithelial	D, R, U	15	Informational technology
30	F	2016	88†	Pleural	Epithelial	A, D, C, I	80	Administrative worker
31	F	2017	53	Pleural	Epithelial	D	23	Cleaner
32	F	2017	76	Pleural	Epithelial	D, C	17	Rehabilitation coordinator
33	F	2017	46	Peritoneal	Epithelial	D	25	Clerical worker

*Tissue analysis presented done by author. Tissue analysis might have been done in some cases by other investigator, these results are not presented in this paper.
†Deceased as of writing; vital status of many individuals is currently unknown.

present.[41,42] Autopsy studies have been performed[43–45] in individuals without a specific history of workplace asbestos exposure; full exposure histories were not obtained. Langer measured asbestos fiber burdens in New York City residents with no known history of asbestos.[46] Roggli and Longo[47] measured tissue burdens for individuals who had bystander or household exposure from family members who directly worked with asbestos in their work, such as laundering clothes. However that type of exposure does not truly reflect background or ''unexposed'' individuals. Lee and Van Orden[32] measured background air exposure in and outside of buildings. They found short chrysotile, tremolite, and actinolite fibers, but no anthophyllite or crocidolite, and very small levels of amosite. Lee and Van Orden's results are consistent with the background asbestos fibers found in the older women the present study.[32] While fiber burden studies are rarely undertaken in the course of clinical treatment, and are used primarily for medico-legal purposes, the findings of various fibers in the lung tissues can provide guidance as to potential prior asbestos exposure, whether from occupation, residential, or para-occupational exposure to asbestos. Attention to true background rates for fiber burdens is critical.[48]

Our findings strongly suggest that asbestos exposure through asbestos-contaminated cosmetic talc explains cases once deemed idiopathic or ''spontaneous,'' and underline the importance of

TABLE 2. Tissue Digestion of Six Mesothelioma Cases

Case	Sex	Mesothelioma Site	Asbestos Type	Site Found	Concentration (Fibers/g) (Lung, Lymph)	Limit of Detection (Lung, Lymph)	Asbestos Bodies
1	F	Pleural	Anthophyllite	Lung	3,286	1,643	0
2	F	Pleural	Anthophyllite, tremolite, actinolite	Lung, lymph node	8,625, 34,500	2,875, 11,500	0
3	F	Pleural	Tremolite	Lung, lymph node	0, 9,409	6,900, 9,409	0, 409
4	F	Peritoneal	Chrysotile	Peritoneum	920	920	0
5	F	Peritoneal	Anthophyllite	Lymph node	20,700	10,350	0, 0
6	M	Pleural	Anthophyllite, tremolite	Lymph node	17,250	3,450	0

TABLE 3. Current Levels of Asbestos Fiber Burden Observed in Digests of Tissue From Autopsy and Surgical Population With no History of Asbestos Exposure (Controls)

Tissue Type	*N*	Asbestos Type	Mean (Fibers/Gram Wet Weight)*	Range (Fibers/Gram Wet Weight)
Lung tissue	35	Chrysotile	892	0–30,000
		Tremolite	84	0–1,552
		Chrysotile and tremolite	35	0–1,208
		Asbestos bodies	<1 bodies/gram wet weight	0–6
Paratracheal or parachronchial lymph node tissue	35	Chrysotile	72	0–1,1035
		Tremolite	29	0–552
		Chrysotile and tremolite	24	0–828
		Asbestos bodies	<1 bodies/gram wet weight	0–5
Peritoneum + gynecological tissue	10	Chrysotile	0	0
		Tremolite	0	0
		Chrysotile and tremolite	0	0
		Asbestos bodies	0	0

*All fibers that were counted were always 1 μm or less in length.

collecting detailed exposure histories that incorporate these findings in patients presenting with mesothelioma. Several factors may hinder the collection of comprehensive exposure histories among individuals diagnosed with mesothelioma. Minimal training in occupational medicine and exposure taking practice among medical students may contribute to a lack of or incomplete exposure history elicitation on the part of clinicians.[49,50] Secondly, long latency periods between exposure and illness pose a challenge both to individual recall as well the ability to establishing causality. Due to the relatively short period between diagnosis and death among mesothelioma patients, patients are often too ill or are deceased before being able to provide a full history. Furthermore, though the presence of asbestos in talc and talcum powder was first discussed in the scientific literature in the 1940s, individuals may not be aware that the products they used contained asbestos. Few clinicians are aware that this is a potential exposure. Typically, patients with mesothelioma will be simply asked whether they worked with or around asbestos, rather than being providing with a listing of potential sources of the types of exposure in which one might encounter asbestos. Cases of mesothelioma among hairdressers characterized as idiopathic also underscore the contribution of an incomplete exposure history; the potential failure to identify the use of talcum powder exposure in their work would prevent the linking of occupational exposure to asbestos to their mesothelioma. In our paper, there were three female hairdressers who regularly used talcum powder in their work. It was unclear from any of the histories noted in the medical records that these women were asked if they used talcum powder as part of the hair cutting process. In a report from the National Mesothelioma Registry of Italy, staff noted a cluster of mesothelioma due to ''unknown exposure'' among hairdressers, but only examined hairdryer use as a potential exposure. There was no discussion of the occupational use of talcum powder.[51] However, McDonald et al,[52] noted that a barber's occupational exposure to asbestos to talc could explain the increased finding of tremolite in the individual's lung fiber burden.

The case series presented should be understood in the context of its limitations. Data were obtained from medication records and transcripts of depositions, rather than structured, in-person interviews. However, the information solicited during the course of the patients' depositions were thorough, and included exhaustive questioning about alternative sources of asbestos exposure, including household exposure, exposures from external industrial sources, occupational exposure, and potential exposure from family members. While deposition testimony is by definition self-report, depositions were given under oath and the potential for recall bias noted would be presented whether patients completed a structured interview or were asked questions during sworn testimony. Furthermore, the utilization of medical records allowed the authors to corroborate important medical information and confirm the pathological diagnosis.

In March 2019 the Federal Drug Administration (FDA) released a statement as an update to their 2017 finding, confirming asbestos contamination of certain cosmetic products marketed and sold to young girls and outlining new steps to work with manufacturers to ensure the safety of their products.[53] While such public acknowledgment of the potential for asbestos contamination in cosmetic talc marks an important turning point, manufacturers are not legally obligated to register cosmetic products with the FDA. The results of this study coupled with the widespread use of such products[26] underline the continued risks posed to consumers through common household and cosmetic products. While these products remain unregulated and on the shelves, the use of talcum powder must be incorporated into standard exposure history practice in order to promote earlier detection of asbestos related disease among non-occupationally exposed individuals. This paper provides evidence that mesothelioma cases once considered idiopathic may be attributable to asbestos-contaminated cosmetic talcum powder usage and that the elicitation of a history of such usage is imperative to obtaining a full exposure history in all patients presenting with mesothelioma.

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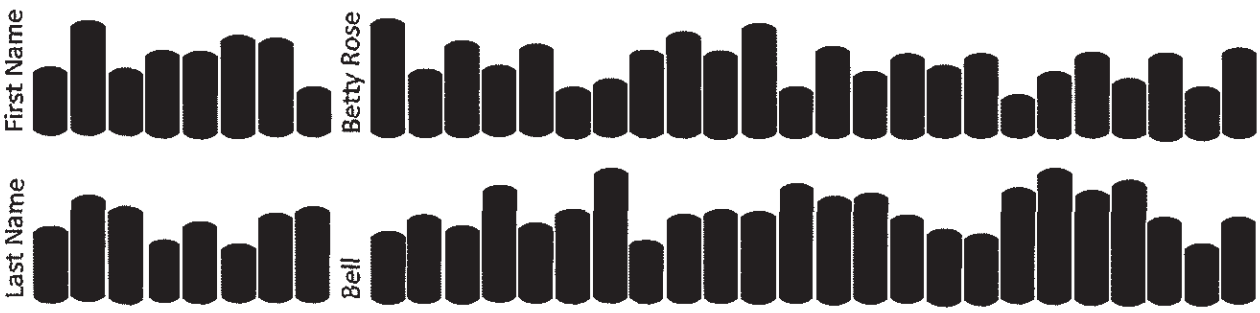
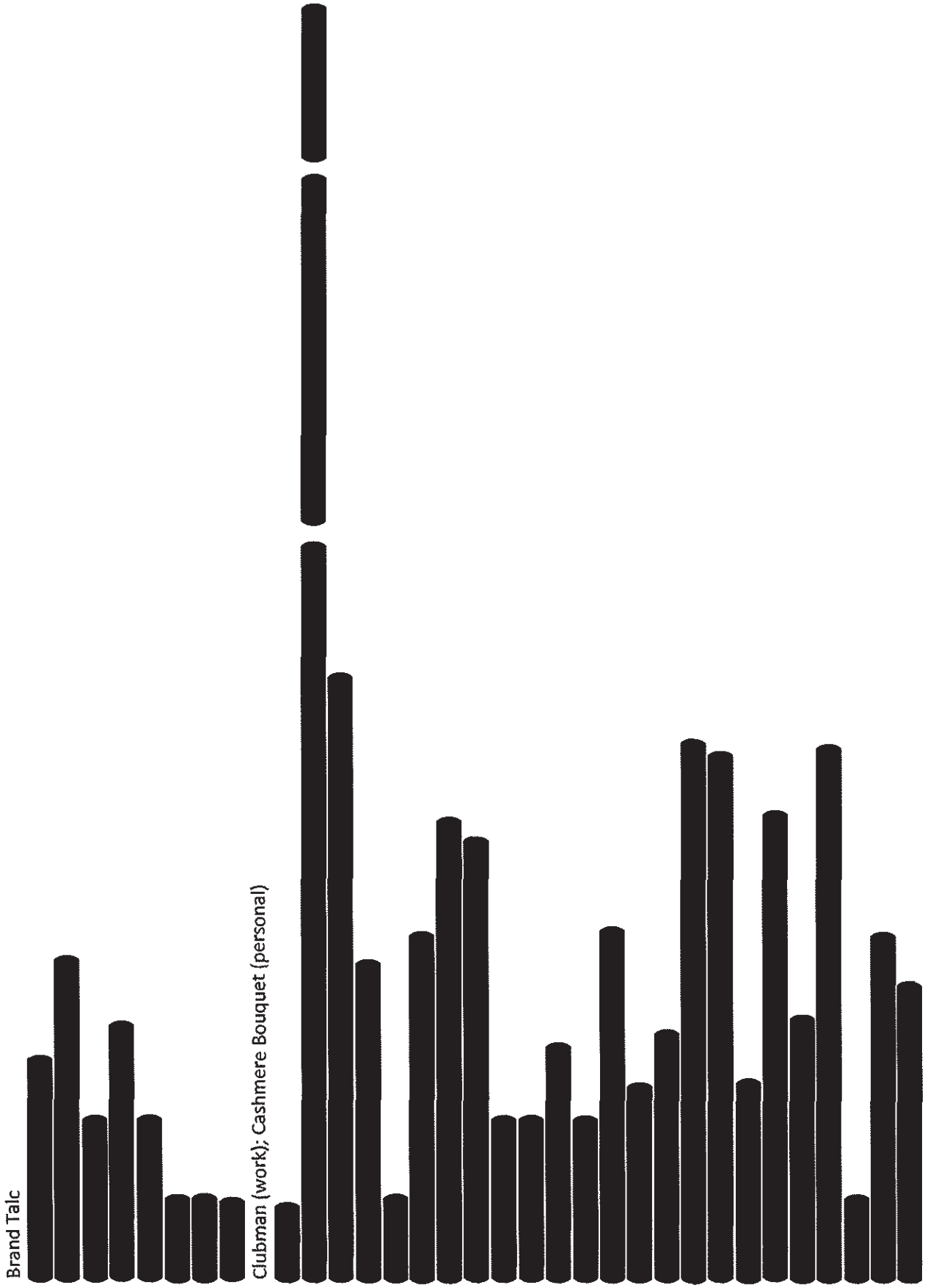
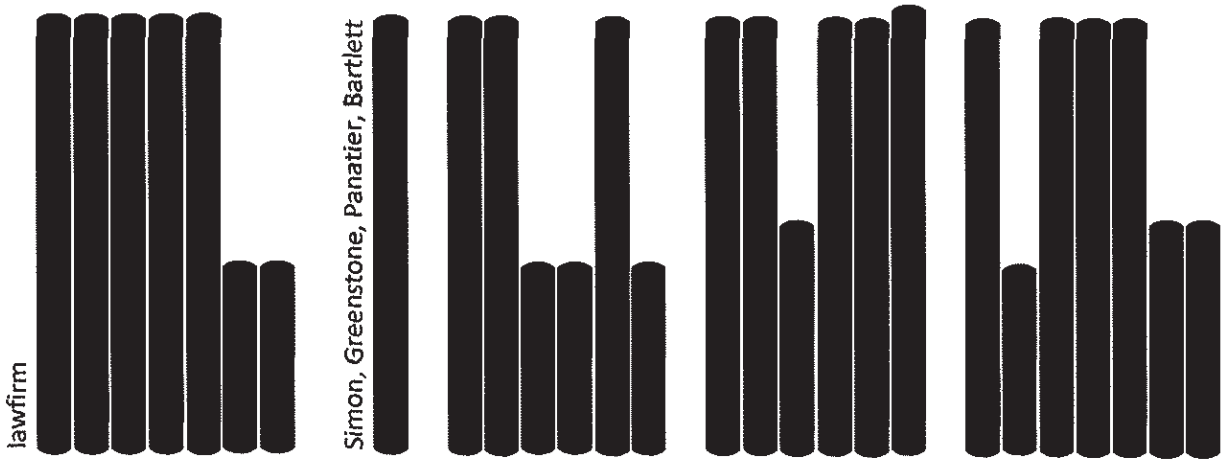
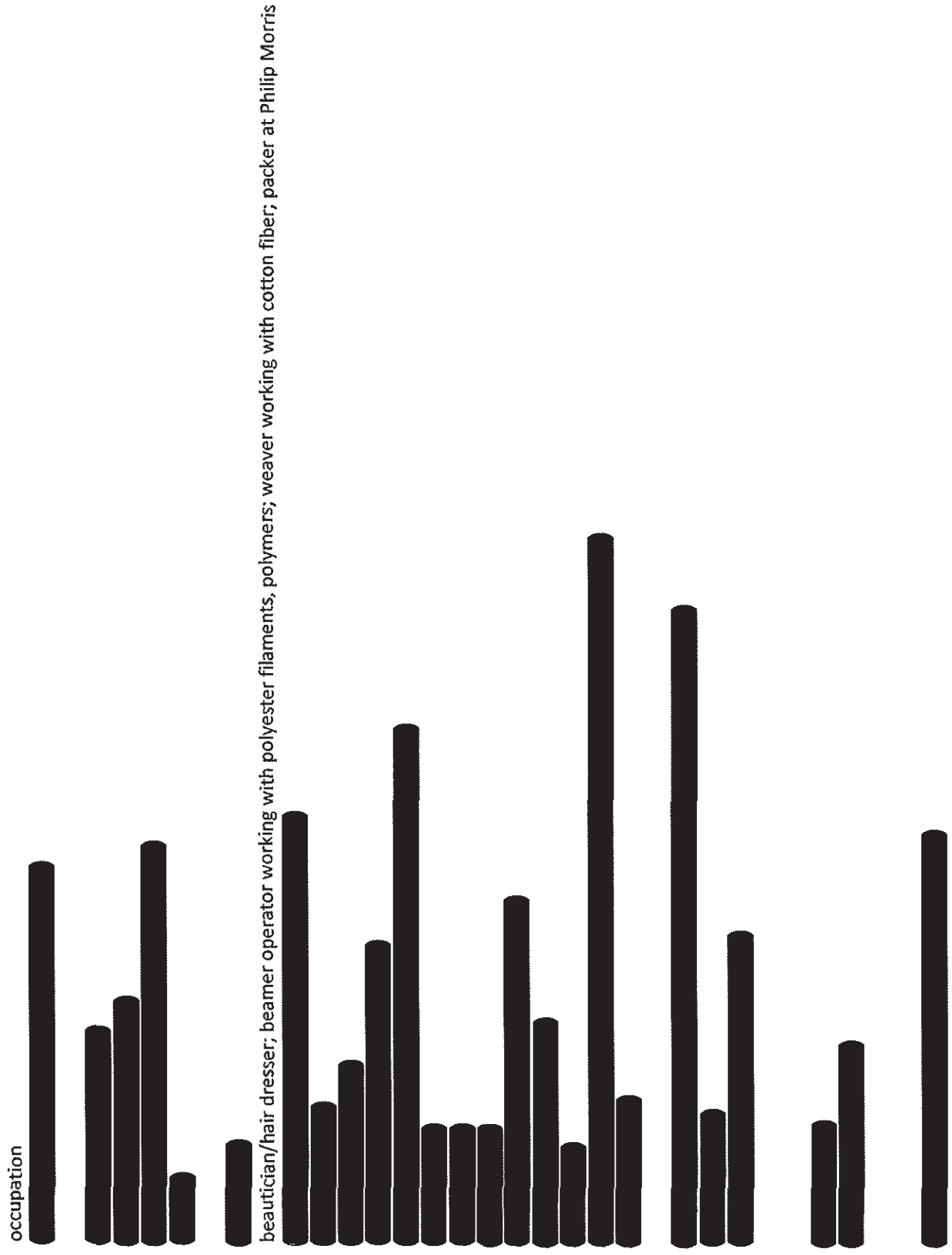
EXHIBIT B








occupation
beautician/hair dresser; beamer operator working with polyester filaments, polymers; weaver working with cotton fiber; packer at Philip Morris

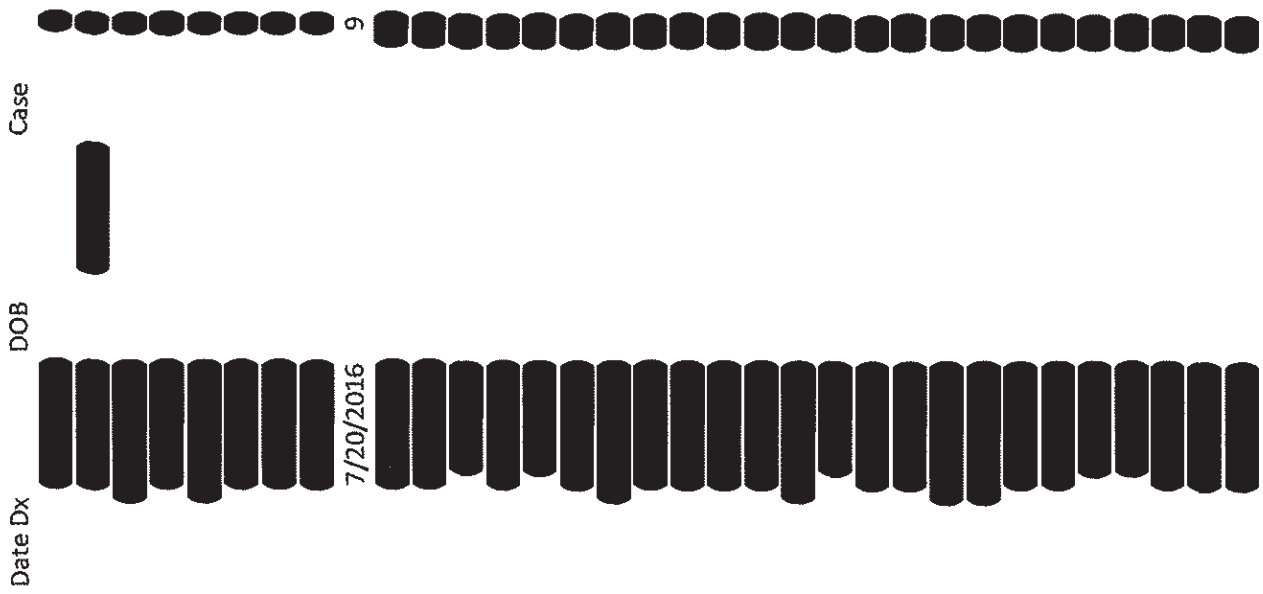


EXHIBIT C

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RESEARCH

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Exposure to cosmetic talc and mesothelioma

Jacqueline Moline[1,2*], Kesha Patel[1] and Arthur L. Frank[3]

Abstract

Aim Mesothelioma is associated with asbestos exposure. In this case series, we present 166 cases of individuals who had substantial asbestos exposure to cosmetic talc products as well as some who had potential or documented additional exposures to other asbestos-containing products and who subsequently developed mesothelioma.

Methods Data were gathered for all subjects referred to an occupational and environmental medicine specialist as part of medicolegal review. Years of total cosmetic talcum powder usage was noted as well as the latency from the onset of talcum powder use to the mesothelioma diagnosis. Alternate asbestos exposure in addition to the exposure from cosmetic talc was categorized as none, possible, likely, and definite.

Results In 122 cases, the only known exposure to asbestos was from cosmetic talc. For 44 cases, potential or documented alternate exposures in addition to the cosmetic talc were described.

Conclusion Cumulative exposure to asbestos leads to mesothelioma; for individuals with mixed exposures to asbestos, all exposures should be considered. Use of cosmetic talc is often overlooked as a source of asbestos exposure. All individuals with mesothelioma should have a comprehensive history of asbestos exposure, including cosmetic talc exposure.

Keywords Malignant mesothelioma, Cumulative asbestos exposure, Cosmetic talcum powder

Introduction

Mesothelioma, described as a sentinel tumor, is intimately associated with asbestos exposure. Asbestos has been used for decades in thousands of products, both in occupational and non-occupational settings, historically accounting for the bulk of mesothelioma cases. Non-occupational exposures can be environmental in nature, from effluents from mines and factories, from para-occupational exposures such as "shade-tree mechanics" using friction products, and from home renovations [1]. Household exposures affecting family members, known as "take-home" exposure has been well described in the literature [2–5]. An underappreciated source of exposure is the use of cosmetic talc products. The International Agency for Research on Cancer (IARC) [6] states that asbestos contaminated talc is carcinogenic and should be treated as if one were dealing with asbestos. Asbestos levels in talcum powder are significantly above background ambient asbestos exposure levels [7–9]. Talc application simulation studies have been published [7, 8] where exposures to talcum powder were 1.9 f/cc and 2.57 f/cc, respectively. According to the Gramond et al. [10] categorization of intensity, asbestos exposure at these levels would be considered to be high (> 1–10 f/ml).

Historically, asbestos exposures at work have been linked to multiple products. The overall risk for asbestos related disease, including mesothelioma, is related to cumulative exposure. As agencies such as NIOSH, OSHA, the EPA, and others have recognized, there is no known safe exposure to asbestos. Low doses of exposure to asbestos contribute to mesothelioma [11].

*Correspondence:
Jacqueline Moline
jmoline@northwell.edu
[1] Department of Occupational Medicine, Epidemiology and Prevention, Northwell Health, Great Neck, NY 11021, USA
[2] Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY 11549, USA
[3] Dornsife School of Public Health of Drexel University, Philadelphia, PA 19104, USA

Both time from first exposure (latency) and total exposure (cumulative dose) to asbestos must be taken into account when evaluating risk. With multiple repeated incidences of exposure, all those above background level should be thought of as "'substantial." When considering the elevated risk of mesothelioma in sheet metal workers [12, 13], Zoloth and Michaels considered the multiple bystander exposures to different products, not simply one construction material. This case series presents 166 cases of individuals who had a minimum of five years and a mean of 40.8 years of exposure to asbestos through cosmetic talc products, some with possible other exposures, but all developed mesothelioma.

Methods

Data were gathered for all subjects referred to an occupational and environmental medicine specialist, JM, as part of medicolegal review. All cases were reviewed personally by an occupational medicine specialist with experience evaluating asbestos exposure in thousands of individuals. The individual's medical records were reviewed and mesothelioma diagnoses were based on pathological reports that were performed as part of their diagnostic evaluation. Exposure data was obtained by sworn testimony of the mesothelioma patients in all cases, and/or from family members who had direct knowledge of the individual's use of cosmetic talc and, if present, other sources of asbestos exposure. Use of talc was recorded as being diapered or powdered as a child; diapering or powdering children or others; applying talcum powder to oneself after bathing, or other personal applications of talc. Years of total cosmetic talcum powder usage was noted as well as the latency from the onset of talcum powder use to the mesothelioma diagnosis. Age was presented within a 10 year window to maintain confidentiality. Data reviewed included family occupational histories (parents or anyone cohabitating with the individual), hobbies, residence, living with or laundering clothes of an asbestos exposed worker, if indicated, home renovations that could have exposed the individual to asbestos containing construction materials, residence close to a facility with environmental contamination, or other potential asbestos exposures. In those individuals with potential asbestos exposure in addition to the cosmetic talc, categorization of these exposures was done by two occupational physicians, JM and ALF. Alternate asbestos exposure in addition to the exposure from cosmetic talc was categorized as none, possible, likely, and definite following the descriptions by Gramond et al. [10]. Non-occupational exposure to asbestos was characterized as paraoccupational (living with an asbestos worker or cleaning clothes), do-it-yourself home repair, domestic (handling asbestos material or living in the presence of asbestos material susceptible to damage at home), or environmental (living near and asbestos processing plant). This study was conducted with approval from the Human Research Protection Program at Northwell Health Feinstein Institute for Medical Research (#21–0897-OTH).

Results

We identified 166 individuals with exposure to cosmetic talc who were diagnosed with a malignant mesothelioma between 2014 and 2021. None of these individuals were previously included in publications by the authors [14]. A summary of the case findings is found in Table 1. Overall, the average age of diagnosis was 63.3 (age range 26–94) years of age. The majority of cases were epithelioid mesothelioma (75.3%). The average length of exposure to cosmetic talc was 40.8 years (range 5–76 years of use), and the average latency period from the onset of talcum powder use to the development of mesothelioma was 52.4 (20—83 years). We identified 122 individuals with asbestos exposure solely through use of cosmetic talc. Exposure to talcum powder could have been for personal use, in an occupational setting (for example, a nurse applying talcum powder to a patient), or applying talcum powder to others such as children. For 122 individuals, they either used cosmetic talc while diapering children or recalled applying talc to others (such as their children). Overall, 80.6% of women and 52.4% of men used talcum powder for diapering or applying talc to others. For 44 individuals, potential alternate asbestos exposure in addition to cosmetic talc was reported. Table 1 presents the 44 cases with alternate exposure ranked by possible, likely, and definite asbestos exposure. Twenty-two women (17.8%) and fifteen men (35.7%) had likely or definite alternate exposure to asbestos in addition to their talcum powder usage. [Details of the exposure history of all 166 individuals with cosmetic talc exposure is presented in Table 2, including a description of the alternate exposure.] Table 1 also shows the site of the tumor by gender. Of the 166 cases, 109 were pleural, 52 were peritoneal, 4 were discovered in both the pleura and peritoneum and the original site could not be determined. One case of pericardial mesothelioma was noted out of the 166 cases, which reflects the rarity of this site for mesothelioma. The percentages of peritoneal mesothelioma were similar for women (29.8%) and men (35.7%). The high proportion of peritoneal mesothelioma tumors relative to pleural tumors, consistent with prior case series of patients with malignant mesothelioma after cosmetic talc use [14, 15], is unusual and deserves further investigation.

Table 1 Characteristics of 166 mesothelioma cases with cosmetic talc usage

		Total ($N=166$)	Female ($n=124$)	Male ($n=42$)
Average Age (range)		63.3 (26 – 94)	64.3 (26 – 94)	60.9 (28 – 83)
Years of Talc Use* **(range)**		40.8 (5 – 76)	40.4 (6 – 76)	42.0 (5 – 74)
Talc Latency in Years (range)		52.4 (20 – 83)	53.3 (20 – 83)	49.9 (28 – 74)
Diapering or Applying Talc to Others**		122 (73.5%)	100 (80.6%)	22 (52.4%)
Talc Use Only		122 (73.5%)	97 (78.2%)	25 (59.5%)
Talc Use and Alternate Exposure		44 (26.5%)	27 (21.8%)	17 (40.5%)
Certainty of Alternate Exposure ($n=44$) (26.5%)	Possible	7 (4.2%)	5 (4.0%)	2 (4.8%)
	Likely	17 (10.2%)	14 (11.3%)	3 (7.1%)
	Definite	20 (12.0%)	8 (6.5%)	12 (28.6%)
Tumor Location	Pleura	109 (65.7%)	83 (66.9%)	26 (61.9%)
	Peritoneum	52 (31.3%)	37 (29.8%)	15 (35.7%)
	Both Pleura & Peritoneum	4 (2.4%)	3 (2.4%)	1 (2.4%)
	Pericardium	1 (0.6%)	1 (0.8%)	0
Tumor Subtype	Biphasic	24 (14.5%)	18 (14.5%)	6 (14.3%)
	Epithelial	125 (75.3%)	92 (74.2%)	33 (78.6%)
	Sarcomatoid	16 (9.6%)	13 (10.5%)	3 (7.1%)
	Not specified	1 (0.6%)	1 (0.8%)	0

* Years of Talc Use: includes years of being diapered or powdered with talc as a child; years of diapering or powdering children or others with talc; and years applying talcum powder to oneself after bathing or other personal use

** Diapering or Applying Talc: restricted to diapering or powdering children with talc or applying talcum powder to others, including occupational use

Discussion

This paper presents 166 individuals with malignant mesothelioma and asbestos exposure through documented use of cosmetic talcum powder. For 122 of 166, their only known exposure to asbestos was their use of cosmetic talcum powder. Without the recognition of asbestos exposure through cosmetic talcum powder, 73.5% of the cases might well have been considered "idiopathic." Similarly, for those 26.5% of cases with additional asbestos exposure along with the talc, those alternate exposures would have been mistakenly considered as the sole, and sufficient, cause of the mesothelioma. Historically, the attributable risk of asbestos for mesothelioma in women ranged from around 20–50%. However as Baur et al. point out, misclassification or inadequate exposure ascertainment has led to this low attributable risk for women compared to men. [16]. Data from occupationally exposed cohorts that included men and women actually show that compared to similarly exposed men, women had higher mortality rates from mesothelioma [17–20]. Lacourt found that at low-level cumulative asbestos exposure ((0 – 0.1 f-cc/year) women were more likely to develop mesothelioma than men [21]. Magnani (2008) found the SMR for mesothelioma was higher for women than for men among workers at an asbestos cement plant [22]. Frank et al. (2009) found mesothelioma rates in the Qingdao region of China were correlated with a higher proportion of women employed in asbestos manufacturing industries. [23] In some instances authors limited the characterization of asbestos exposure in women to certain industries, such as shipbuilding during wartime [24], thus neglecting other potential sources and decreasing the attributable risk. Conversely, when non-occupational exposures were included for women, even with low-intensity domestic exposure considered, the attributable risk increased from 40% to 64.8% [21].

Given that all types of asbestos can cause mesothelioma [6], it is important to consider every source of exposure to asbestos in an individual. Talcum powder has been contaminated with both chrysotile and amphibole asbestos (predominately anthophyllite and tremolite) [8, 25, 26]. Recently, Wong et al. (2021) found significantly elevated risks of mesothelioma among individuals with only chrysotile exposure and for mixed fiber exposure. [27]. Chrysotile alone (OR = 3.8) and in combination with tremolite/anthophyllite asbestos (OR = 3.9) were associated with similar increases in risk of mesothelioma. These three fiber types are most commonly found in cosmetic talc, and given that different ore sources were used in manufacturing over time, it is likely that many formulations and uses of talcum powder involved mixed fiber type exposure. There is no scientific basis to state that one type of exposure was the sole cause of the mesothelioma in a mixed exposure scenario. For example, rates of mesothelioma have been evaluated based on either job type or locale (e.g., construction, shipping) rather than

Table 2 Description of 166 mesothelioma cases

Age at Diagnosis	Sex	Tumor Location	Tumor Subtype	Occupation(s)	Talc Latency (years)	Years of Talc Use*	Diapering/ Applying Talc to Others**	Certainty of Alternate Exposure	Type of Alternate Exposure
51–60	F	Pleura	Epithelial	Cosmetics factory	41	36	Yes	None	
31–40	F	Peritoneal	Biphasic	Marketing	39	12	No	None	
91–100	F	Pleura	Epithelial	Clerical worker	69	57	Yes	Definite	Smoked Kent cigarettes in 1950s
51–60	M	Pleura	Biphasic	Warehouse supervisor	54	22	No	Definite	Home renovations as child
21–30	M	Peritoneal	Epithelial	Aircraft technician	28	5	No	None	
41–50	F	Pleura	Biphasic	Marketing	47	47	Yes	Definite	Automotive friction exposure
41–50	F	Peritoneal	Epithelial	Operator technician	37	36	Yes	Likely	Parents worked in chemical plant/with automotive friction materials; no work clothes laundered at home
61–70	F	Peritoneal, pleura	Epithelial	Hairdresser	65	57	Yes	Definite	Household exposures laundering clothes (automotive friction materials)
41–50	F	Pleura	Epithelial	Industrial engineer	45	10	Yes	None	
71–80	M	Pleura	Biphasic	Firefighter, painter	59	59	No	Definite	Occupational exposures to industrial talc, firefighting
51–60	F	Peritoneal	Epithelial	Dental assistant, secretary, logging business	58	57	Yes	Definite	Automotive friction product exposure
51–60	F	Peritoneal, pleura	Epithelial	Nurse	50	20	Yes	None	
71–80	F	Pleura	Epithelial	Secretary	60	61	No	None	
61–70	M	Peritoneal	Epithelial	Software engineer	53	53	No	Likely	Construction work as teenager; family member machinist
61–70	F	Pleura	Epithelial	Secretary	61	20	Yes	None	
61–70	M	Pleura	Epithelial	Law professor	46	45	No	None	
21–30	F	Peritoneal	Biphasic	Customer service manager	26	12	No	None	
51–60	F	Pleura	Epithelial	Dental assistant, sales	50	17	Yes	Likely	Dental tape used in office
21–30	F	Pleura	Epithelial	Programmer	29	17	Yes	None	
51–60	F	Pleura	Epithelial	Clerical worker	54	48	No	None	
71–80	F	Pleura	Biphasic	Dental assistant, receptionist	64	34	Yes	Possible	Possible household exposure from parental occupations
61–70	F	Pleura	Epithelial	Systems analyst	62	61	Yes	None	

Table 2 (continued)

Age at Diagnosis	Sex	Tumor Location	Tumor Subtype	Occupation(s)	Talc Latency (years)	Years of Talc Use*	Diapering/ Applying Talc to Others**	Certainty of Alternate Exposure	Type of Alternate Exposure
51–60	F	Peritoneal	Epithelial	Clerical worker	59	31	Yes	Likely	Asbestos shingle exposure as child
71–80	F	Peritoneal	Epithelial	Teacher's aide, customer service	46	46	No	None	
51–60	M	Pleura	Epithelial	Baked goods manufacturer	55	49	Yes	None	
61–70	F	Pleura	Epithelial	Housekeeping, packaging	51	23	No	None	
41–50	M	Peritoneal	Epithelial	Lawyer	46	23	Yes	None	
51–60	M	Pleura	Sarcomatoid	IT	30	30	Yes	None	
61–70	F	Peritoneal	Epithelial	Bookkeeper	62	15	Yes	None	
71–80	M	Pleura	Epithelial	Engineer	71	20	No	Definite	Home renovations, automotive friction products, cement in molds
41–50	F	Pleura	Epithelial	Restaurant	46	12	No	None	
81–90	F	Pleura	Epithelial	Not provided	62	62	Yes	Likely	Household exposures laundering clothes (automotive friction materials)
81–90	F	Pleura	Epithelial	LPN	67	18	Yes	Likely	Household exposures laundering clothes (automotive friction materials)
31–40	F	Peritoneal	Epithelial	Nanny, teacher	26	7	Yes	Definite	Home renovations
61–70	M	Peritoneal	Epithelial	Packaging, machine operator, welding	48	48	Yes	Definite	Cut transite and cement pipes; automotive friction exposure ("shade tree")
71–80	F	Peritoneal	Biphasic	Clerical worker	61	39	Yes	None	
51–60	F	Peritoneal	Epithelial	Lawyer	54	18	No	None	
41–50	F	Pleura	Sarcomatoid	Research	44	45	Yes	None	
51–60	F	Peritoneal	Epithelial	Variety of jobs	50	48	Yes	Definite	Home renovation
41–50	M	Peritoneal	Epithelial	Farrier, mechanic, general labor	41	35	Yes	Definite	Occupational exposure
81–90	M	Pleura	Epithelial	Barber	50	36	Yes	Likely	Boiler work in rail yards
71–80	M	Pleura	Biphasic	Bus driver, factory worker	47	47	Yes	None	
51–60	F	Peritoneal	Epithelial	Physician	20	12	Yes	None	
61–70	F	Pleura	Epithelial	Cashier, sales, clerical worker, wire assembler	53	53	No	None	
51–60	F	Peritoneal	Epithelial	Laborer	41	50	Yes	Likely	Home renovations, family member worked with clay

Table 2 (continued)

Age at Diagnosis	Sex	Tumor Location	Tumor Subtype	Occupation(s)	Talc Latency (years)	Years of Talc Use*	Diapering/ Applying Talc to Others**	Certainty of Alternate Exposure	Type of Alternate Exposure
61–70	M	Pleura	Epithelial	Accountant	69	69	Yes	Definite	Home renovations during 1970s
81–90	F	Pleura	Biphasic	Bookkeeping, rehab counseling	83	32	Yes	None	
71–80	F	Pleura	Sarcomatoid	Office manager	75	75	Yes	None	
61–70	F	Pleura	Epithelial	Merchandising manager	31	18	Yes	None	
41–50	F	Pleura, peritoneal	Epithelial	Teacher	46	22	Yes	None	
51–60	M	Pleura	Epithelial	Automechanic, pipefitter	31	44	Yes	Definite	Occupational and take home exposure (shipyard)
51–60	F	Peritoneal	Epithelial	Clerical worker	40	38	Yes	None	
41–50	F	Pericardium	Sarcomatoid	Medical center	50	31	Yes	None	
71–80	M	Pleura	Epithelial	Mechanic, parts manager	61	50	No	Definite	Occupational naval exposure to asbestos, automotive friction material handling
71–80	F	Pleura	Epithelial	Secretary, cosmetics, cashier	50	25	No	Definite	Household exposures laundering clothes (automotive friction materials)
61–70	F	Pleura	Sarcomatoid	Catering	45	40	Yes	None	
61–70	F	Pleura	Epithelial	Cleaner, personal assistant	52	50	Yes	None	
51–60	M	Pleura	Epithelial	Meat inspector	41	26	No	None	
71–80	F	Pleura	Epithelial	Office manager	65	55	Yes	Possible	Household exposure from husband (drilling wells, pipes)
71–80	F	Pleura	Epithelial	Clerical worker	60	59	Yes	Possible	Family member worked at service station (no details on work)
71–80	M	Pleura	Sarcomatoid	Accountant	47	39	Yes	None	
61–70	F	Pleura	Epithelial	Sales, business	60	16	No	None	
81–90	M	Peritoneal	Epithelial	Accountant	68	56	No	None	
51–60	F	Pleura	Epithelial	Social worker	40	6	No	None	
71–80	F	Pleura	Epithelial	Hairdresser	60	49	Yes	None	
41–50	M	Pleura, peritoneal	Epithelial	Warehouse worker	47	8	No	Definite	Automotive filler exposure
51–60	F	Pleura	Epithelial	Retail, bankteller, work at school	56	56	Yes	None	
61–70	F	Pleura	Biphasic	Bakery	64	49	Yes	None	
71–80	F	Pleura	Epithelial	Hospitality	61	58	Yes	None	
51–60	F	Pleura	Epithelial	Cashier	57	56	Yes	None	
81–90	F	Peritoneal	Epithelial	Teacher	40	50	Yes	Possible	Abatement done at work

Table 2 (continued)

Age at Diagnosis	Sex	Tumor Location	Tumor Subtype	Occupation(s)	Talc Latency (years)	Years of Talc Use*	Diapering/ Applying Talc to Others**	Certainty of Alternate Exposure	Type of Alternate Exposure
81–90	F	Pleura	Epithelial	Physical therapy assistant	64	62	Yes	None	
31–40	M	Peritoneal	Epithelial	IT	35	25	No	None	
51–60	F	Pleura	Epithelial	Housekeeper	42	34	Yes	None	
81–90	F	Pleura	Epithelial	Teacher	54	50	Yes	Likely	Home renovations
61–70	M	Pleura	Epithelial	Accounting	63	63	Yes	None	
71–80	M	Pleura	Epithelial	Tractor driver, race track	62	60	No	Likely	Oil drilling
71–80	F	Pleura	Epithelial	Research	62	42	Yes	None	
51–60	F	Peritoneal	Epithelial	Agriculture consultant	53	53	Yes	None	
31–40	F	Peritoneal	Epithelial	Clerical worker	39	27	Yes	None	
41–50	F	Pleura	Biphasic	Clerical worker	49	49	No	Likely	Ceramics use
71–80	M	Pleura	Epithelial	Communications system/ office	47	49	Yes	None	
81–90	F	Pleura	Not specified	Nurse	76	70	Yes	Likely	Family member worked in shipyard
71–80	F	Peritoneal	Epithelial	Meat wrapper	56	47	Yes	None	
71–80	M	Pleura	Biphasic	Advertising	62	62	Yes	None	
71–80	F	Peritoneal	Epithelial	Teacher, hospital administration	70	70	Yes	None	
41–50	M	Peritoneal	Epithelial	Chef	37	36	No	None	
51–60	F	Peritoneal	Epithelial	Case manager	53	52	Yes	None	
41–50	F	Peritoneal	Epithelial	Finance and marketing	42	34	No	None	
51–60	M	Pleura	Epithelial	Painter, carpet installer	38	38	Yes	Definite	Automotive friction product use
81–90	F	Pleura	Epithelial	Secretary	63	45	Yes	None	
71–80	F	Pleura	Epithelial	Nursing	69	40	Yes	None	
51–60	F	Peritoneal	Epithelial	Nurse	46	22	Yes	None	
41–50	M	Peritoneal	Epithelial	Industrial engineer	48	53	Yes	None	
71–80	F	Peritoneal	Epithelial	Librarian	55	44	Yes	None	
51–60	F	Pleura	Biphasic	Clerical worker, hostess	53	15	No	None	
71–80	F	Pleura	Epithelial	Secretary	67	55	Yes	None	
71–80	F	Pleura	Epithelial	Clerical worker	64	20	Yes	None	
71–80	F	Peritoneal	Sarcomatoid	Secretary, medical billing	47	47	Yes	None	
81–90	F	Pleura	Epithelial	Communications and real estate	69	69	Yes	None	
41–50	F	Peritoneal	Epithelial	Home health	42	24	Yes	None	
51–60	F	Pleura	Biphasic	Clerical worker, hostess	53	15	Yes	None	
71–80	F	Pleura	Biphasic	Therapy aid	67	67	Yes	None	
61–70	M	Pleura	Biphasic	Restaurant, lead technician	50	47	Yes	None	
61–70	F	Pleura	Sarcomatoid	Teacher	51	43	Yes	None	

Table 2 (continued)

Age at Diagnosis	Sex	Tumor Location	Tumor Subtype	Occupation(s)	Talc Latency (years)	Years of Talc Use*	Diapering/ Applying Talc to Others**	Certainty of Alternate Exposure	Type of Alternate Exposure
51–60	F	Pleura	Epithelial	Sales	44	16	Yes	None	
41–50	F	Pleura	Epithelial	Chicken farming, medical assistant	48	48	Yes	None	
41–50	M	Peritoneal	Epithelial	Physician	40	17	No	None	
71–80	F	Pleura	Epithelial	Secretary	69	64	No	None	
61–70	F	Pleura	Epithelial	Assembly line worker	51	52	Yes	None	
61–70	F	Pleura	Epithelial	X-ray technician	40	40	Yes	None	
51–60	F	Pleura	Biphasic	Factory worker, housekeeper	33	14	Yes	None	
51–60	F	Pleura	Epithelial	Clerical worker	38	29	Yes	None	
61–70	F	Pleura	Epithelial	Clerical worker	54	27	Yes	None	
81–90	F	Pleura	Epithelial	Variety of jobs	76	76	Yes	None	
71–80	F	Peritoneal	Epithelial	Receptionist, dental assistant	45	35	Yes	None	
71–80	F	Pleura	Epithelial	Midwife	55	47	Yes	None	
81–90	F	Pleura	Epithelial	Seamstress	63	56	Yes	None	
71–80	F	Peritoneal	Epithelial	Accounting	65	65	Yes	None	
61–70	F	Pleura	Epithelial	Nurse	57	57	Yes	None	
71–80	M	Peritoneal	Epithelial	Sales, truck driver	45	32	No	Definite	Automotive friction products use
51–60	M	Pleura	Epithelial	Lawyer	48	48	Yes	None	
51–60	F	Pleura	Sarcomatoid	Customer service	56	27	Yes	None	
81–90	F	Pleura	Sarcomatoid	Teacher	53	47	Yes	None	
71–80	F	Peritoneal	Epithelial	Not provided	67	48	No	Definite	Smoked Kent cigarettes in 1950s
31–40	F	Peritoneal	Biphasic	Banking	39	19	Yes	None	
71–80	M	Pleura	Epithelial	Logger, run loader	74	74	Yes	Possible	Automotive friction product use and home renovations
71–80	F	Peritoneal	Epithelial	Hairdresser	50	50	Yes	Likely	Hairdryers present in salon
31–40	F	Pleura	Sarcomatoid	Certified Nursing Assistant and phlebotomist	39	24	Yes	None	
71–80	F	Pleura	Epithelial	Seamstress	62	52	Yes	None	
31–40	F	Peritoneal	Epithelial	Variety of jobs	27	20	Yes	None	
61–70	F	Pleura	Epithelial	Laborer	51	51	Yes	None	
41–50	M	Peritoneal	Biphasic	Casino worker	47	47	Yes	None	
81–90	F	Pleura	Epithelial	Nurse	67	18	Yes	None	
71–80	M	Pleura	Epithelial	Accountant, comptroller	70	30	Yes	Possible	Home renovations
61–70	F	Pleura	Sarcomatoid	Clerical worker	60	27	No	None	
61–70	F	Pleura	Biphasic	Secretary, cleaner	52	52	Yes	Likely	Home renovations in 1970s

Table 2 (continued)

Age at Diagnosis	Sex	Tumor Location	Tumor Subtype	Occupation(s)	Talc Latency (years)	Years of Talc Use*	Diapering/ Applying Talc to Others**	Certainty of Alternate Exposure	Type of Alternate Exposure
61–70	F	Pleura	Sarcomatoid	Office cleaner, food prep	64	64	Yes	None	
61–70	F	Pleura	Epithelial	Insurance agent	58	57	Yes	None	
71–80	F	Pleura	Epithelial	Cook, cleaner, concierge	54	44	Yes	None	
31–40	M	Peritoneal	Epithelial	Lab technician	36	36	No	None	
91–100	F	Pleura	Epithelial	Variety of jobs	60	60	No	None	
51–60	F	Pleura	Epithelial	Real estate broker	36	35	Yes	None	
41–50	F	Pleura	Biphasic	PhD in astronomy, dance teacher	37	37	No	None	
71–80	F	Pleura	Epithelial	Switchboard operator, HR	64	50	No	None	
51–60	F	Peritoneal	Epithelial	Nurse	50	46	Yes	Likely	Ceramics work for 4–5 years
41–50	F	Peritoneal	Epithelial	Lawyer	44	20	No	None	
71–80	F	Pleura	Epithelial	Quality control	67	67	Yes	None	
51–60	F	Pleura	Sarcomatoid	Counselor	55	54	No	None	
71–80	F	Pleura	Biphasic	Certified nursing assistant, ranch work	62	35	Yes	Likely	Vermiculite exposure
71–80	M	Peritoneal	Epithelial	Physician	67	67	Yes	None	
41–50	F	Peritoneal	Epithelial	Nurse Practitioner	44	34	Yes	None	
31–40	M	Pleura	Epithelial	Not provided	29	30	No	None	
61–70	F	Pleura	Epithelial	Banking	60	50	Yes	None	
51–60	F	Peritoneal	Epithelial	Nurse	56	45	Yes	None	
71–80	F	Pleura	Sarcomatoid	Hairdresser	61	25	Yes	None	
71–80	M	Pleura	Sarcomatoid	Mechanic	60	48	No	Definite	Occupational exposure and home renovations
61–70	M	Peritoneal	Epithelial	Worked at special education preschool	57	50	No	None	
71–80	F	Peritoneal	Biphasic	Teacher	65	46	Yes	None	
71–80	F	Pleura	Biphasic	Teacher	71	59	Yes	Possible	Family member was Linotype operator
81–90	F	Pleura	Epithelial	Cashier, waitress	60	58	Yes	None	
31–40	F	Pleura	Epithelial	Administrator	28	7	No	None	
71–80	F	Peritoneal	Epithelial	Teacher	50	51	Yes	Likely	Household exposure to laundry (automotive friction materials)
31–40	M	Pleura	Epithelial	Homeland Security	33	33	No	None	
61–70	M	Pleura	Epithelial	Trucking company	55	56	Yes	None	
71–80	F	Pleura	Epithelial	Office worker	62	45	Yes	None	

* Years of Talc Use: includes years of being diapered or powdered with talc as a child; years of diapering or powdering children or others with talc; and years applying talcum powder to oneself after bathing or other personal use

** Diapering or Applying Talc: restricted to diapering or powdering children with talc or applying talcum powder to others, including occupational use

on each specific task or exposure within the job category. Furthermore, mesothelioma is a disease that occurs following a long latency period. It is important to consider whether the latency period for all exposures, whether due to asbestos in talcum powder, or through occupational or para-occupational exposures meets the minimum latency period.

Subgroups of individuals not traditionally known to be exposed to asbestos have been identified, such as teachers. In this case series, 12 teachers (7.2% of cases) were diagnosed with mesothelioma. Anderson et al. identified 12 school teachers with mesothelioma in Wisconsin (6 male, 6 female). [28]. Nine cases had no known exposure to asbestos, although several worked in school buildings with asbestos containing building materials (ACBM) present, but the condition of the ACBR while the teachers were present in the school was unknown. No history of talcum powder use was elicited. Marianaccio et al. identified mesotheliomas in 11 female teachers in Italy. [29]. Mazurek et al. evaluated mesothelioma deaths in women in the United States from 1999–2020 using death certificate data. [30]. Mesothelioma was noted in 32 female elementary and middle school teachers. No information on exposure to asbestos or specific tasks at work or a comprehensive exposure history was available; no history of talcum powder use was elicited, as the study was based solely on death certificates. Tomasallo et al. found increased mortality among school teachers in Wisconsin, USA. [31]. They noted that para-occupational or take home exposure could be responsible for the increased risk. Again, no history of asbestos exposure through talcum powder usage was ascertained. It might be possible that exposure to ACBM played some role in these mesotheliomas, however, the notable history of exposure to asbestos-containing talcum powders among teachers in this case series, highlights the importance of assessing this source of exposure in future studies of mesothelioma in teachers and other predominantly female professions.

Mazurek et al. found seven cases of mesothelioma among female hairdressers. [30]. Our series identified five hairdressers/barbers with documented occupational exposure to asbestos containing talcum powder. Moline et al. found three hairdressers who used cosmetic talc as part of their occupation, [14] and Emory et al. [15] found 4 hairdressers out of 75 patients. Pavlisko et al. identified a hairdresser in their study of mesothelioma in women, but classified the case in the non-occupational/paraoccupational exposure category. [32] McDonald attributed the finding of tremolite in the lung tissue of a chrysotile worker to his prior occupational exposure to talc as a barber [33]. Rodelsberger recognized talc as a source of asbestos exposure and identified hairdressers and barbers as asbestos-exposed industries [34]. The examples of these two occupational subgroups, teachers with personal use of cosmetic talc, and hairdressers with occupational use of cosmetic talc, show the importance of obtaining a thorough history and determining all potential sources of asbestos exposure.

This case series describes mesotheliomas in end-users of cosmetic talcum powder, thus using no personal protective equipment or dust suppression activities, unlike some cohorts with occupational exposures [35]. Prior mortality studies of talc miners and millers in Italy (and other countries) have not identified mesotheliomas in their populations, although two cases of peritoneal cancer were identified by Pira et al. [36]. The Rubino, Coggiola and Pira et al. studies used mortality data collected prior to an ICD mesothelioma code, which could impact proper classification of mesothelioma. [35–37]. The studies had a relatively small sample size, which given the rarity of mesothelioma, even among highly exposed individuals, would have led to insufficient statistical power [38]. Fordyce studied Vermont talc miners and found two mesotheliomas in the small cohort of 427 miners; Vermont talc has been used in cosmetic talcum powder [39].

Fiber burden studies were done in some individuals from the two prior case series of mesothelioma among individuals with cosmetic talcum powder use. Moline et al. reported on tissue fiber analysis in six of 33 individuals. Asbestos fibers, of the types found in cosmetic talc, were found in all six samples. Emory et al. found anthophyllite asbestos in all 9 individuals for whom tissue fiber analysis was done. Tremolite was found in six of the cases in addition to the anthophyllite. Hull et al. [40] looked at New York State talc miners and found anthophyllite, tremolite/actinolite, chrysotile and talc in their lungs. There were over a dozen cases of mesothelioma identified in these talc miners. Our case series did not include data on tissue sampling, which is not typically done for clinical purposes; rather we relied on patient history. For occupational exposures to asbestos, fiber analysis is not required to ascertain a history of exposure, rather the history of exposure to asbestos is sufficient [41]. This should be no different for environmental exposures, such as asbestos exposure in cosmetic talcum powder, or even para-occupational exposures.

Pleural mesothelioma is more common than peritoneal mesothelioma [42], with estimates of pleural mesothelioma occurring approximately 80–90% of the time compared to peritoneal mesothelioma. The presenting location for the tumor, either pleural or peritoneal, was similar in all three recent case series. In Moline et al., 11 of 33 patients had peritoneal mesothelioma and in Emory et al., 23 of 75 cases were peritoneal mesothelioma. In this larger case series, the proportion of peritoneal mesotheliomas was 31.3%. The proportion of men

in each of the three case series was similar. In Emory et al., 15% of the cases were men, compared with 18% of the cases in Moline et al. In the current case series, among 122 cases with talc-only exposure, 20.5% were men, slightly above the proportion in two previous case series. This might reflect growing awareness among men that talcum powder use could explain their mesothelioma, particularly when no other identifiable source of asbestos was identified. Few individuals in this case series underwent testing for the tumor suppressor gene, BAP-1, which is associated with an increased risk for mesothelioma when associated with asbestos exposure, [43] including greater susceptibility at low doses of asbestos such as exposures from cosmetic talcum powder use. Interestingly, there was a greater frequency of peritoneal mesothelioma cases in those with the BAP-1 mutation and asbestos exposure [44].

Several authors have written about the importance of the cumulative dose, which has been related to several asbestos-caused diseases, both non-malignant and non-malignant. Luberto et al. discussed the "increased mortality risk due to asbestos exposure for malignant neoplasm of pleura, peritoneum, lung and ovary, as well as asbestosis, all increasing with cumulative exposure." [19] Henderson et al. commented on the use of the cumulative exposure model in the Helsinki Criteria. [45] Iwastsubo and colleagues, citing only low exposures leading to disease noted that "excess of mesothelioma was observed for levels of cumulative exposure." [46] Ferrante and her colleagues [47] found that the "risk of pleural malignant mesothelioma increased with cumulative asbestos exposure and also in analyses limited to subjects non-occupationally exposed," comparable to the current case series. Albin et al. [48] even noted that "colorectal cancer displayed a clear relation with cumulative dose," as one would reasonably expect with asbestos-related diseases.

This case series may reflect the potential sources of bias that impact all studies that use cases in which litigation is occurring. However, because mesothelioma is a rare disease and full environmental histories are rarely obtained or documented, it would be impossible to amass so many cases with one type of exposure using standard sources such as hospital or cancer registry records. Furthermore, most patients (and their clinicians) are unaware of the presence of asbestos in talcum powder, leading them to report no known asbestos exposure. The data related to years of exposure to cosmetic talcum powder was obtained and typically described in great detail during sworn testimony. For nearly one-quarter of the individuals in this series, additional exposures to asbestos were reported along with the cosmetic talcum powder. When available, information regarding talcum powder usage was corroborated by sworn testimony of family members. Typically, the questioning of individuals about alternate exposures to asbestos as part of litigation is fairly comprehensive, but it is possible that there were additional, unknown sources. This presents a challenge for any study of asbestos exposure and, in particular, mesothelioma, given the long latency period from the onset of exposure to the development of disease.

Conclusion

For individuals with exposure to asbestos through cosmetic talc usage and additional alternate sources, all exposures contribute to the development of mesothelioma. Published case reports and case series have identified over 100 individuals whose sole exposure to asbestos was through cosmetic talcum powder usage [14, 15, 49]. Thus, is it critical to obtain a history of all potential exposures to asbestos. In this case series, 122 cases would have had no source of asbestos identified if a history of asbestos-containing cosmetic talc had not been elicited. The other 44 would have likely been misclassified as having only alternate exposures. It is indisputable that asbestos causes mesothelioma, therefore, it is critical to elicit all potential sources of asbestos exposure so that we can better understand, and prevent, future cases of this deadly cancer.

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Authors' contributions
Jacqueline Moline conceived of the manuscript, and was involved in the acquisition of data, analysis and writing of the manuscript. Kesha Patel was involved in data presentation and analysis. Arthur L. Frank was involved in writing and evaluation of alternative exposures. The author(s) read and approved the final manuscript.

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Availability of data and materials
The datasets generated and/or analyzed during the current study are not publicly available. Individuals of details of cases will not be provided to protect the confidentiality of the cases presented in the study. Efforts to minimized identification, such as describing age in a range were employed.

Declarations

Ethics approval and consent to participate
The project received approval from the Institutional Review Board and we received a waiver of consent to include the participants in the study. (IRB #: 21–0897).

Consent for publication
Not applicable.

Competing interests
Authors Jacqueline Moline and Arthur L. Frank have served as expert witnesses in asbestos litigation, including talc litigation for plaintiffs.

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Publisher's Note

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PROOF OF SERVICE

(This section should not be filed with the court unless required by Fed. R. Civ. P. 45.)

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